

Date: February 11, 2005

RESPONSE TO DETAILED ACTION

1. It is acknowledged that the term of "use" should not have been applied. The term "method" was the correct term as intended.
2. We have attached a listing of Figures modified with sequence references attached.

ELECTIONS/ RESTRICTIONS

3. We elect restriction to Group I. Group II/III are process claims, which are presently withdrawn. We will elect to rejoin the process claims to the product claims in an amendment when/if the product claim is determined to be allowable.
4. We acknowledge the definition of product and process claims as distinct inventions.
5. Restriction is accepted.
6. We will elect to rejoin the process claims to the product claims in an amendment when/if the product claim is determined to be allowable.

We submit the following amended Figures to include sequence references.

Fig.3 shows diagram and DNA sequence of chimeric hMN14 sFv IgTCR, including the CD8 α hinge modified-to-remove cysteines, within a retroviral vector. The IgTCR molecule specified in this invention occupies nucleotides 2426 to 3766. (Sequence ID No.1 [the vector sequences are incidental] **and Sequence ID No.2.**)

Fig.4 shows the DNA sequence of the VH domain (4A) (Sequence ID No.3 and No.4) and VL domain (4B) (with attached Ck sequences) (Sequence ID No.5 and No.6) that are specific to hMN14. These sequences were modified to prepare the sFv used in Fig.1 and Fig.3, and similarly for other constructs.

We submit the following amended claims:

What is claimed is:

1. (presently amended) A chimeric molecule comprised of the CEA binding domain of humanized antibody MN14 as a single chain antibody with a (GGSGS)₃ linker (residues 127-141 of Sequence ID No.2), the zeta signaling chain of the T cell receptor and an intervening CD8 α hinge in which the cysteine residues have been mutated, with the sequence of Figure 3 **(Sequence ID No.1 and No.2).**
2. (previously presented) A molecule of claim 1 in which other signaling chains of T cells or other cell types are substituted, or in which a different hinge molecule or no hinge molecule is substituted, or a combination thereof.
3. (previously presented) A molecule of claim 1 or 2 in which at least one of the CDRs of the heavy chain of MN14 and one of the CDRs of the light chain of MN14 are preserved in a form (e.g., sFv or Fab) that maintains the binding of the CEA antigen, and/or in which the linker is of different composition.
4. (previously presented) A molecule of claim 1, 2 or 3 which has been modified in DNA or protein sequence but which retains the specificity and action of these molecules.
5. **(presently amended and withdrawn)** ~~The use of~~ **methods of applying** molecules of claims 1, 2, 3 or 4 expressed in T cells or NK cells or other effector cells to treat patients with cancers expressing the CEA antigen.
6. **(presently amended and withdrawn)** The **methods of applying in** combination **the** molecules of claims 1, 2, 3 or 4 expressed in T cells or NK cells or other effector cells to treat patients with cancers expressing the CEA antigen, together with each other or with heterologous constructs to engage additional stimulatory and functional properties of the effector cells to enhance the antitumor therapeutic efficacy.